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Muscle Tone Suppression and Stepping Produced by Stimulation of Midbrain and Rostral Pontine Reticular Formation

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Stimulation of the midbrain retrorubral (RRN), ventral paralemniscal tegmental field (vFTP), reticular tegmental (TRN), and pedunculopontine tegmental (PPN) nuclei was found to produce bilateral suppression of muscle tone in the unanesthetized, decerebrate animal. The RRN is the most rostral area shown to produce such suppression. This muscle tone suppression was frequency- and intensity-dependent. At low stimulus intensities, bilateral suppression was produced at these sites. At higher current and frequency levels, 2 types of muscle responses were found, excitation in PPN and RRN and initial suppression followed by excitation in TRN and vFTP. The mean latency to muscle tone suppression was not significantly different in TRN (36.8 msec) and RRN (36.5 msec). However, muscle tone suppression latency was significantly shorter in vFTP (31 msec) and PPN (27.1 msec). In addition to muscle tone suppression, stepping-like activity could be elicited at the same points by consecutive train stimulations in PPN and single train stimulation in TRN and vFTP. Thus, systems producing atonia are colocalized with those producing locomotion. We hypothesize that the midbrain atonia regions control more caudal regions producing muscle tone suppression in REM sleep, and that the locomotor and atonia eliciting regions are normally coactivated during REM sleep.

Spinal circuits produce motoneuron hyperpolarization during rapid eye movement (REM) sleep (Chase, 1983; Chase et al., 1986). Horseradish peroxidase (HRP) retrograde transport, electrophysiological, and lesion studies have indicated that these spinal circuits are controlled by medial medullary neurons that innervate the ventral horn of the spinal cord through the ventrolateral funiculus (Sakai et al., 1979; Tohyama et al., 1979; Kanamori et al., 1980; Schenkel and Siegel, 1989). Stimulation of the medial medulla, including the magnocellularis and paramedianus nuclei, produces muscle tone suppression (Magoun and Rhines, 1946; Lai and Siegel, 1988). It has been hypothesized that this medullary region is controlled by the pontine peri-locus coeruleus α (peri-LCα) (Sakai et al., 1981; Chase, 1983; Morales et al., 1987; Siegel et al.,. 1989). Cholinergic stimulation of the peri-LCα and immediately adjacent regions in decerebrate or chronic intact cats produces REM sleep-like electroencephalographic (EEG) activity and muscle atonia (George et al., 1964; Katayama et al., 1984; Shiromani et al., 1986; Lai and Siegel, 1988). However, regions rostral to the peri-LCα have not been shown to be capable of producing muscle tone suppression.

Cells in the peri-LCα and adjacent pontine region receive a major input from the pedunculopontine (PPN) nucleus (Mitani et al., 1988; Shiromani et al., 1988). Webster and Jones (1988) have shown that destruction of cells in the PPN region produces REM sleep without atonia. Therefore, we hypothesized that stimulation of the PPN would produce suppression of muscle tone. In the present study, we tested this hypothesis and also explored more rostral midbrain regions for atonia elicitation. We found that stimulation of the midbrain retrorubral (RRN), ventral paralemniscal tegmental field (vFTP), reticular tegmental nucleus (TRN), and PPN produced bilateral suppression of muscle tone.

Materials and Methods

Twenty-one adult cats, of either sex, weighing 2.2–6.0 kg were decerebrated at postmammillary-precollicular level as described previously (Lai et al., 1987). Core temperature was maintained at 38 ± 1°C by a thermoregulated heating pad. Blood pressure was monitored and mean arterial blood pressure remained over 80 mm Hg in all preparations. Electrical stimulation was delivered through a stainless steel monopolar microelectrode, with tip size of 0.01 in. (Model 5710, A-M Systems) between A3 and P2, L0 and 6.0, H+2 and −9 (Berman, 1968) in 0.5 mm increments. Constant current trains (500 msec duration, 0.2 msec rectangular cathodal pulses) with varied intensity and frequency were used. Stimulation experiments began 10 or more hr after decerebration. Electromyograms were recorded bilaterally from occipitoscapularis, triceps brachii, and splenius muscles with stranded stainless wires (Cooner Wire Co.), insulated except for 3 mm at the tip. Stimulus-triggered averages were computed using 300 msec (100 Hz) trains for determining the latency, duration, and magnitude of the muscle inhibition. The onset of muscle suppression was defined as the point of inflection below baseline values.

Results

Areas that produced bilateral inhibition of muscle tone are shown in Figure 1. Stimulation of more rostral regions, specifically of the substantia nigra, did not produce muscle tone suppression.

The latency of muscle tone suppression was shortest in PPN (27 msec) and vFTP (31 msec), and relatively longer in TRN (37 msec) and RRN (37 msec) (Table 1). The differences in latency values were significant ($p < 0.01$, F test). The present pontine and midbrain latency values can be compared with latencies of 16.5 msec to muscle tone suppression that we have found after stimulation in the medial medulla (Y. Y. Lai and J. M. Siegel, unpublished observations; Lai et al., 1987).

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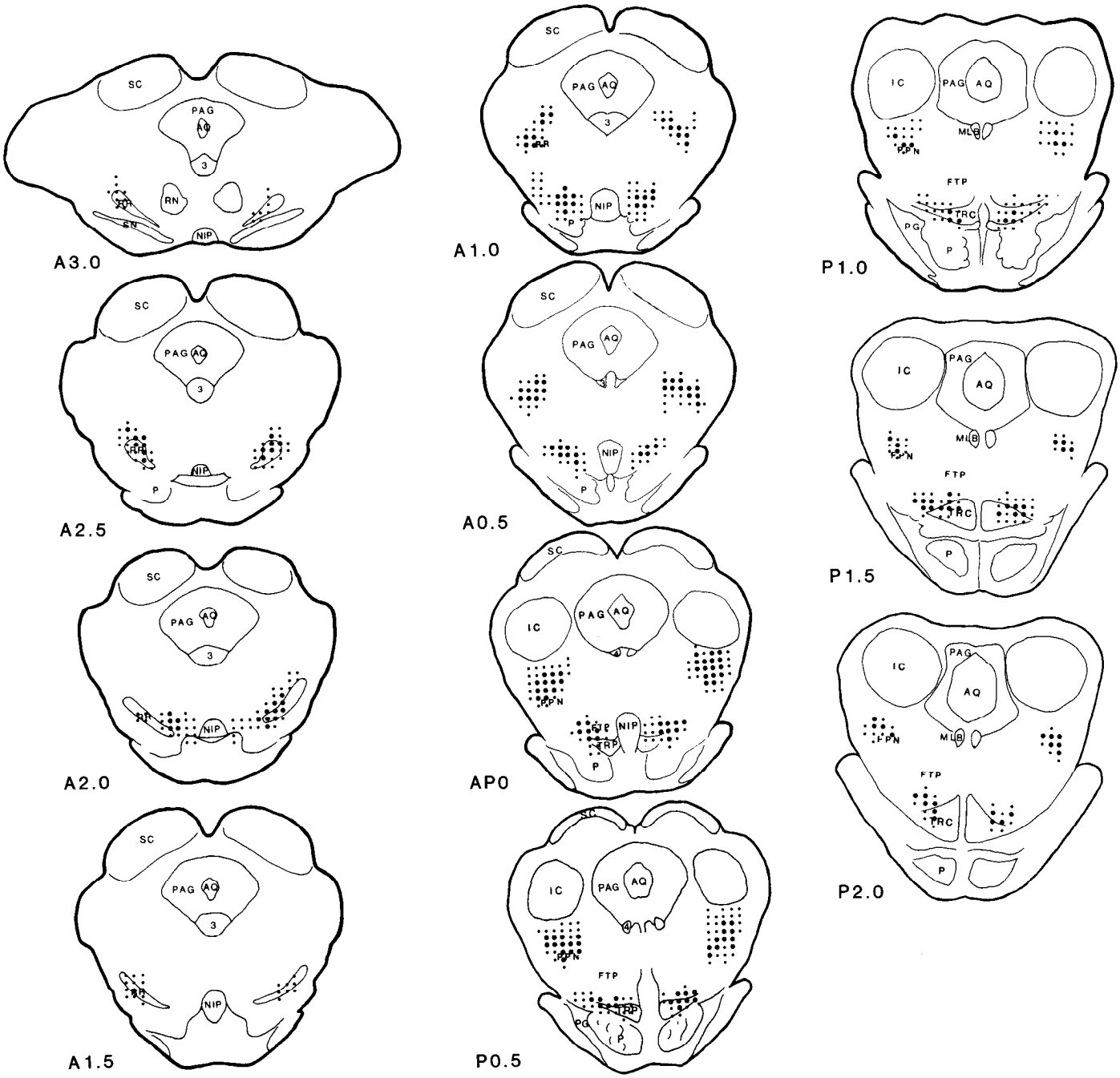


Figure 1. Location of the pontomesencephalic inhibitory area in decerebrated cats. Data are summarized from 14 animals; 500 msec train with 100 Hz, 0.2 msec, and 10–100 μA rectangular cathodal pulses was applied from A3.0 to P2.0, L0 to 6.0, and H+2.0 to −9.0. *Large* and *small dots* represent the stimulating points that produced ≥ or ≤70% inhibition of neck muscle tone, respectively (compared to 60 sec baseline values, as determined by 10 sec integrations of rectified EMG activity). *3,* Oculomotor nucleus; *4,* trochlear nucleus; *AQ,* aqueduct; *IC,* inferior colliculus; *FTP,* paralemniscal tegmental field; *MLB,* medial longitudinal bundle; *NIP,* interpeduncular nucleus; *P,* pyramidal tract; *PAG,* periaqueductal gray; *PG,* pontine gray; *PPN,* pedunculopontine tegmental nucleus; *RN,* red nucleus; *RR,* retrorubral nucleus; *SC,* superior colliculus; *SN,* substantia nigra; *TRC,* TRN (tegmented reticular nucleus), central division; *TRP,* TRN, pericentral division.

Muscle tone suppression was intensity- and frequency-dependent. Tables 2–5 show results from sites stimulated with frequencies ranging from 5 to 150 Hz. The current threshold (T) for muscle tone suppression and atonia did not differ among the 4 areas stimulated. Muscle response to low frequency stimulation (≤20 Hz) was variable at all sites tested, with inhibition, excitation, or no response seen. The current used at low frequencies varied from 50 to 600 μA. As the current increased, small reductions in tone could be observed. However, complete muscle atonia was never found with low frequency stimulation, even as the intensity was increased up to 600 μA. When the frequency was above 30 Hz, the threshold for atonia showed an intensity-frequency relationship. The threshold for muscle inhibition and current for inducing atonia were decreased as the frequency increased (Tables 2–5).

Although the current threshold for muscle suppression in the

Table 1. Latency of muscle suppression by electrical stimulation in pontomesencephalic and medullary nuclei

Nucleus	Latency (msec) Mean	Range	n_1	n_2
MMRF	16.5 ± 9.7	5–38	82	23
PPN	27.1 ± 10.1	5–45	28	8
vFTP	31.0 ± 16.7	10–60	55	11
TRN	36.8 ± 18.5	5–70	68	13
RRN	36.5 ± 12.8	10–60	74	14

n_1, Number of muscles averaged.
n_2, Number of sites stimulated.

4 areas found to produce atonia was not significantly different, muscle response to higher intensity stimulation was different. With higher intensity stimulation, initial inhibition followed by facilitation during the train was seen in some sites of all 4 nuclei. However, when stimulation intensity was further increased, muscle response was found to be reversed to facilitation in PPN and RRN but not in TRN and vFTP (Tables 2–5). For example, 80 Hz train stimulation was applied to PPN in 1 cat. The threshold to produce muscle tone suppression was 50 μA. As the current increased to 75 μA (1.5 T), stimulation produced complete atonia; 120 μA (2.4 T) produced initial inhibition followed by facilitation and 150 μA (3 T) produced complete facilitation. On the other hand, no facilitation without prior inhibition could be seen in TRN and vFTP with stimulation at 80 Hz, even with intensities as high as 5 T.

Consecutive stimulation trains produced stepping-like activity after the initial muscle tone suppressions at many sites. This is illustrated in Figure 2, where 20 consecutive trains at 100 Hz and 50 μA were applied to the PPN at an intertrain interval of 13.3 sec. The first 17 stimulations produced complete atonia. This inhibitory effect disappeared by the 18th train and was replaced by stepping-like activity. Two minutes after cessation of stimulation, bilateral suppression of muscle tone was again elicited with the previously effective stimulation parameters.

A second type of stimulation-induced stepping-like activity was found in vFTP and TRN. Unlike the stimulation-induced stepping-like activity in Figure 2, which was seen only after *repeated* stimulation trains, the locomotor activity at these sites was present at the *first* stimulation (Fig. 3). A unilateral inhibitory effect on the muscle tone was found to start at H−4.5, corresponding to the midbrain reticular formation. Stepping-like activity began at H−5.0. Bilateral atonia was found between H−6.5 and −7.0 (TRN) even though stepping-like activity was present between the trains. At H−7.5, stimulation-elicited muscle inhibition disappeared, while stepping-like activity still occurred. This locomotor activity lasted for up to 2 min after cessation of stimulation. We never saw stepping activity without prior stimulation. Both consecutive and single train stimulation-induced locomotion were seen only 10 hr or more after decerebration.

Discussion

In the present study, we found that stimulation of RRN, vFTP, TRN, and PPN produced bilateral inhibition of muscle tone in decerebrate cats. Stepping-like activity could be elicited by single train stimulation in vFTP and TRN or after multiple trains in PPN.

PPN and vFTP stimulation produced inhibition at shorter latency than stimulation of TRN and RRN. We also note that stimulation of the medial medulla produced inhibition at shorter latency than all these mesopontine sites. Thus, the present data are consistent with a relay between mesopontine structures and the medial medulla in the induction of muscle tone suppression. The RRN has been shown to project to the PPN (Moon Edley and Graybiel, 1983; Lee et al., 1988), which in turn projects to the peri-LCα (Mitani et al., 1988; Shiromani et al., 1988) and medial medulla (Gerrits and Voogd, 1986; Shiromani et al., 1990). Direct projections from TRN to the medial medulla have

Table 2. Frequency and current dependence of muscle response to PPN stimulation

Frequency (Hz)	Total no. of sites stimulated	T		Atonia		−, +		+	
		n	μA	n	μA	n	μA	n	μA
5	7	1	300	0	—	0	—	0	—
10	7	2	250 ± 00	0	—	1	300	0	—
20	7	6	207 ± 126	0	—	1	400	2	550 ± 50
30	7	7	163 ± 71	5	210 ± 61	5	380 ± 98	1	600
40	7	7	124 ± 52	6	177 ± 64	4	366 ± 107	1	600
50	7	7	96 ± 32	7	158 ± 68	7	278 ± 97	2	450 ± 50
60	7	7	81 ± 24	7	124 ± 39	6	237 ± 75	1	300
70	7	7	73 ± 18	7	102 ± 34	7	187 ± 56	1	250
80	7	7	54 ± 12	7	90 ± 23	6	148 ± 52	2	175 ± 25
90	7	7	45 ± 12	7	62 ± 24	7	119 ± 22	1	250
100	7	7	32 ± 11	7	46 ± 16	6	108 ± 31	2	160 ± 20
120	7	7	28 ± 10	7	39 ± 9	7	89 ± 27	3	126 ± 38
150	7	7	24 ± 8	7	32 ± 6	7	79 ± 21	3	83 ± 47

T, Threshold. Atonia, Complete suppression of muscle tone in all muscles responding, without any muscle facilitation during the train. −, +, Initial suppression followed by facilitation of muscle tone during the stimulation train. +, Facilitation only during stimulation train. n, Number of sites tested for threshold, or exhibiting atonia, or −+ pattern or + pattern.

Table 3. Frequency and current dependence of muscle response to RRN stimulation

Frequency (Hz)	Total no. of sites stimulated	T		Atonia		−, +		+	
		n	μA	*n*	μA	*n*	μA	*n*	μA
10	4	0	—	0	—	0	—	0	—
20	4	0	—	0	—	0	—	0	—
30	4	0	—	0	—	0	—	0	—
40	4	3	136 ± 104	3	240 ± 127	1	550	2	600
50	4	4	128 ± 111	4	208 ± 86	2	525 ± 25	3	583 ± 24
60	4	4	115 ± 87	4	174 ± 72	3	433 ± 24	2	575 ± 25
70	4	4	96 ± 48	4	159 ± 70	2	375 ± 25	2	550
80	4	4	82 ± 45	4	131 ± 66	4	338 ± 41	3	566 ± 24
90	4	4	67 ± 34	4	104 ± 52	3	312 ± 54	2	475 ± 25
100	4	4	52 ± 21	4	82 ± 44	4	287 ± 41	3	466 ± 24
120	4	4	41 ± 26	4	73 ± 32	4	250 ± 35	4	387 ± 21
150	4	4	35 ± 18	4	51 ± 22	2	225 ± 25	2	375 ± 25

also been demonstrated (Gerrits and Voogd, 1986). Direct PPN-spinal projections could also mediate these effects (Goldsmith and van der Kooy, 1988).

The PPN overlaps with the caudal portion of the "mesencephalic locomotion region" (MLR), which has repeatedly been found to produce stepping locomotion when continuous or very long (10 sec) electrical stimulation trains (Shik et al., 1966; Sinnamon, 1984) or chemical microinjection (Garcia-Rill et al., 1985) was applied to it in the decerebrate cat placed on a treadmill. In the intact rat, carbachol injection in the dorsomedial part of the PPN increases, while injection in the ventrolateral part of the PPN decreases locomotion (Milner and Mogenson, 1988). Furthermore, the lateral part of PPN, where we find maximal inhibitory effects, projects to the pontis oralis and caudalis nuclei, ventral part of nucleus reticularis gigantocellularis (Moon Edley and Graybiel, 1983; Kelland and Asdourian, 1989), and nucleus paramedianus (Shiromani et al., 1990), which have been demonstrated by electrical and chemical stimulation to produce bilateral inhibition of muscle tone (Magoun and Rhines, 1946; Lai et al., 1987; Lai and Siegel, 1988).

The TRN has also been hypothesized to be a part of the locomotion system (Chesire et al., 1982; Sinnamon, 1984). Electrolytic lesion or local application of τ-aminobutyric acid in TRN causes rapidly accelerating forward locomotion in rats (Cheng et al., 1981). The inhibitory effect of TRN on locomotion may be mediated by its link with the nucleus paramedianus of the caudal medulla. We have shown that ACh applied to nucleus paramedianus produces muscle atonia (Lai and Siegel, 1988). Anterograde tritiated leucine (Gerrits and Voogd, 1986) and HRP retrograde (Shiromani et al., 1990) transport studies have shown that fibers from TRN and adjacent vFTP project to the nucleus paramedianus in the cat. Lesion studies have suggested that this area has excitatory as well as inhibitory effects on locomotion (Chesire et al., 1983). This is consistent with the

Table 4. Frequency and current dependence of muscle response to TRN stimulation

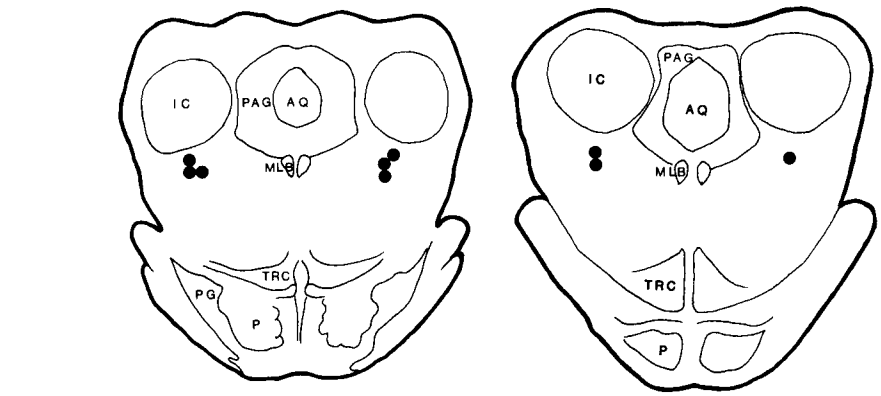
Frequency (Hz)	Total no. of sites stimulated	T		Atonia		−, +		+	
		n	μA	*n*	μA	*n*	μA	*n*	μA
5	5	0	—	0	—	0	—	0	—
10	5	0	—	0	—	0	—	0	—
20	5	1	250	1	500	0	—	0	—
30	5	4	283 ± 129	1	300	0	—	0	—
40	5	5	182 ± 92	2	325 ± 125	0	—	0	—
50	5	5	140 ± 49	4	275 ± 128	0	—	0	—
60	5	5	118 ± 41	5	187 ± 124	0	—	0	—
70	5	5	97 ± 39	5	141 ± 96	1	200	0	—
80	5	5	78 ± 32	5	118 ± 54	1	200	0	—
90	5	5	59 ± 34	5	94 ± 53	1	140	0	—
100	5	5	47 ± 29	5	84 ± 51	2	210 ± 140	0	—
120	5	5	46 ± 26	5	69 ± 47	3	227 ± 121	0	—
150	5	5	38 ± 24	5	56 ± 42	3	182 ± 137	0	—

Table 5. Frequency and current dependence of muscle response to vFTP stimulation

Frequency (Hz)	Total no. of sites stimulated	T		Atonia		−, +		+	
		n	μA	*n*	μA	*n*	μA	*n*	μA
10	2	0	—	0	—	0	—	0	—
20	2	1	300	0	—	0	—	0	—
30	2	2	275 ± 25	1	350	1	600	0	—
40	2	2	200 ± 20	2	325 ± 125	1	600	0	—
50	2	2	160 ± 20	2	290 ± 30	2	525 ± 25	0	—
60	2	2	120 ± 10	2	210 ± 30	1	400	0	—
70	2	2	105 ± 15	2	170 ± 20	2	325 ± 25	0	—
80	2	2	85 ± 5	2	120 ± 10	2	250 ± 25	0	—
90	2	2	75 ± 5	2	100 ± 10	2	225 ± 25	0	—
100	2	2	60 ± 10	2	85 ± 5	1	180	0	—
120	2	2	55 ± 5	2	75 ± 5	2	135 ± 15	0	—
150	2	2	45 ± 5	2	60 ± 10	1	120	0	—

present results showing both locomotion and muscle tone inhibition after stimulation of this region.

The RRN is an area with dopamine-containing neurons (Deutch et al., 1988) located in the ventral mesencephalic tegmentum; it forms a bridge between A9 substantia nigra and A10. HRP and antidromic stimulation studies have shown that the RRN has major projections to TRN (Hayakawa and Zyo, 1986), globus pallidus, caudate putamen (Miller et al., 1983; Steinfels et al., 1983; Deutch et al., 1988; Lee et al., 1988), nucleus accumbens, and central nucleus of amygdala (Preston et al., 1981). The RRN receives projections from nucleus pontis oralis (Vertes and Martin, 1988), PPN (Hallanger and Wainer, 1988), and the central nucleus of the amygdala (Chesselet, 1985; Wallace et al., 1989). Thus, the anatomy, and the physiological findings in the present study, are consistent with a RRN role in the integration of descending limbic influences with motor out-



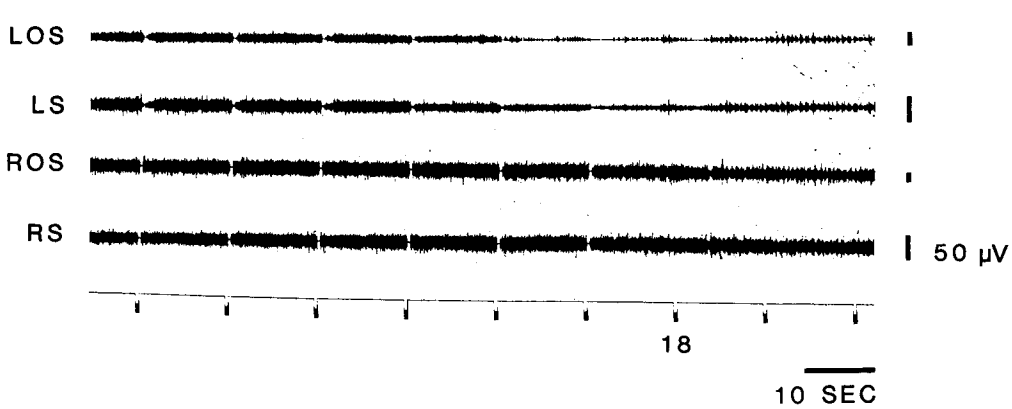


Figure 2. Top, Areas that produce *both* muscle tone suppression and stepping activity with *consecutive* train stimulations. *Bottom,* Twenty consecutive 300 msec trains (100 Hz, 0.2 msec, and 50 μA rectangular cathodal pulses) were delivered to the left side of the brain stem at AP0, L4.5, H−1.0 corresponding to the pedunculopontine nucleus. Muscle inhibition could be seen in the first 17 consecutive train stimulations. No inhibitory response to the stimulation was seen after the 18th stimulation; however, stepping-like activity could be seen. *LOS* and *ROS,* Left and right occipitoscapularis; *LS* and *RS,* left and right splenius.

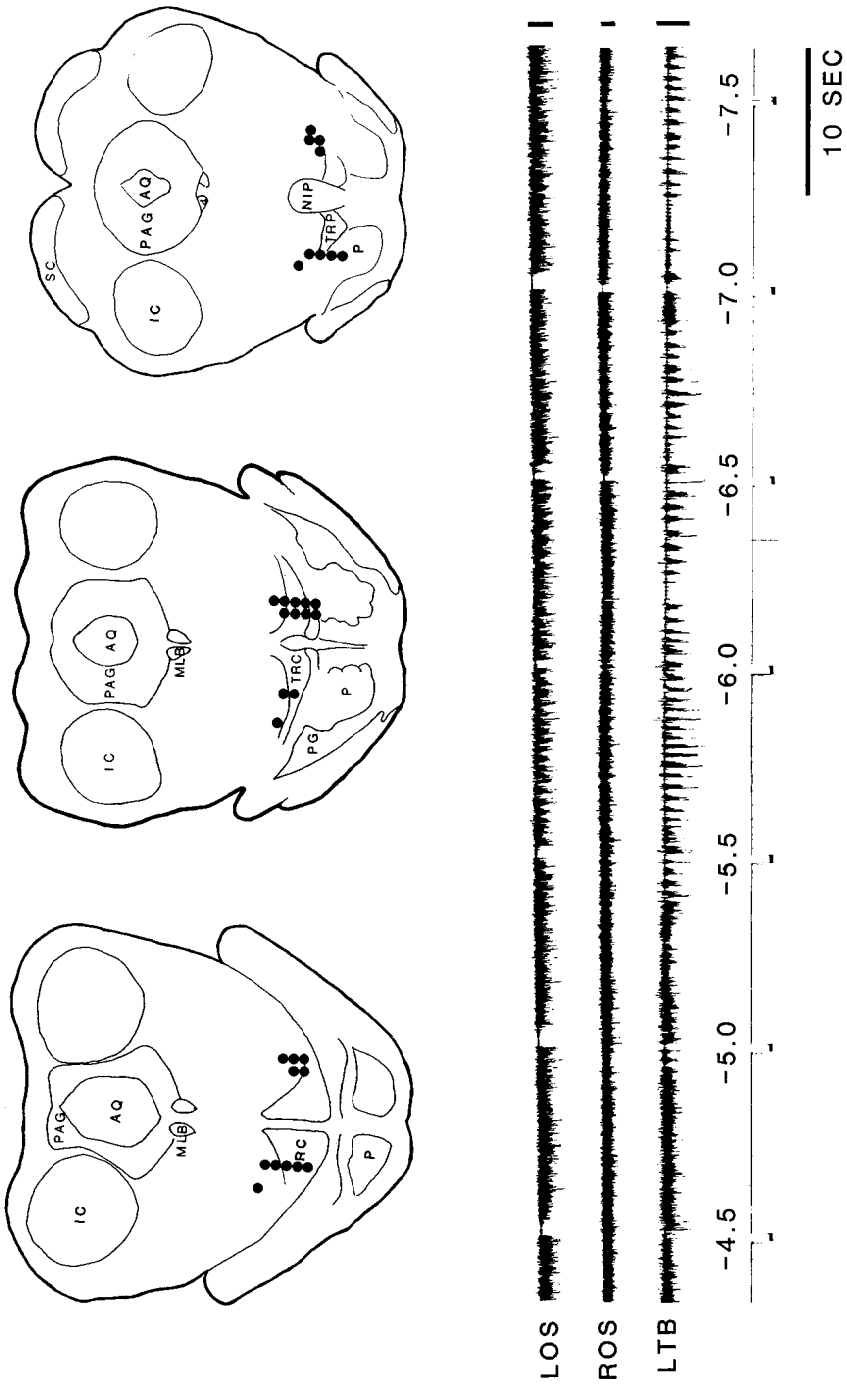


Figure 3. *Top,* Sites that produce *both* muscle tone suppression and stepping activity with *single* train stimulations. *Bottom,* Train stimulation of 500 msec was delivered to the right side of brain stem at A1.0, L2.0, and H+2.0 to −9.0 in 0.5 mm steps. Numbers indicate stereotaxic depth of stimulation. TRP is between H−6 and −7. Stimulation produced unilateral inhibition of muscle tone and induced stepping-like activity 10 sec after H−4.5 stimulation. At −6.5 and −7.0, electrical stimulation produced bilateral inhibition of muscle tone while the stepping-like activity was still present. *LTB,* Left triceps brachii.

put. Cataplexy is the sudden loss of muscle tone in narcoleptics that can be triggered by sudden excitement or strong emotions. It is thought to result from the triggering, in waking, of the REM sleep atonia mechanism. The narcoleptic animal has elevated levels of dopamine receptors in the caudate nucleus, nucleus accumbens, and central nucleus of the amygdala (Baker and Dement, 1985; Mefford et al., 1983; Bowersox et al., 1987), the very regions that receive projections from the retrorubral area. In contrast, the substantia nigra, the other major locus of brainstem dopaminergic neurons, has only a minor projection to the amygdala and shows no activity change in relation to sleep-waking states (Steinfels et al., 1983; Deutch et al., 1988). On the basis of the present results, we hypothesize that the dopamine receptor upregulation of narcolepsy is a consequence of impaired dopamine release from the retrorubral area.

The anatomical proximity of zones producing atonia and stepping may be relevant to the recently discovered REM sleep behavior disorder (Mahowald and Schenck, 1989), a disorder in which vigorous motor activity occurs during a REM sleep state characterized by an incomplete inhibition of muscle tone. We hypothesize that in normal REM sleep, PPN and TRN neurons mediating motor activation and atonia are costimulated, leading to activation of central motor systems (Siegel, 1979; Chase and Morales, 1983; Morrison, 1983) with concurrent motoneuron hyperpolarization blocking the expression of this activity. We further hypothesize that in the REM sleep behavior disorder, developmental or degenerative processes produce a shift of synaptic drive from PPN and TRN neurons mediating atonia to adjacent neurons mediating locomotion, causing the expression of motor activity in REM sleep. Investigation of these rostral regions should be productive in the analysis both of the normal control of muscle tone and of the REM sleep–associated pathologies in this control.

References

Baker T, Dement WC (1985) Canine narcolepsy-cataplexy syndrome: evidence for an inherited monoaminergic-cholinergic imbalance. In: Brain mechanisms of sleep (McGinty DJ, Drucker-Colin R, Morrison A, Parmeggiani PL, eds), pp 199–234. New York: Raven.

Bowersox SS, Kilduff TS, Faull KF, Zeller-DeAmicis L, Dement WC, Ciaranello RD (1987) Brain dopamine receptor levels elevated in canine narcolepsy. Brain Res 402:44–48.

Chase MH (1983) Synaptic mechanisms and circuitry involved in motoneuron control during sleep. Int Rev Neurobiol 24:213–258.

Chase MH, Morales FR (1983) Subthreshold excitatory activity and motoneuron discharge during REM periods of active sleep. Science 221:1195–1198.

Chase MH, Morales FR, Boxer PA, Fung SJ, Soja PJ (1986) Effect of stimulation of the nucleus reticularis gigantocellularis on the membrane potential of cat lumbar motoneurons during sleep and wakefulness. Brain Res 386:237–244.

Cheng JT, Schallert T, De Ryck M, Teitelbaum P (1981) Galloping induced by pontine tegmentum damage in rats: a form of "parkinsonian festination" not blocked by haloperidol. Proc Natl Acad Sci USA 78:3279–3283.

Chesire RM, Cheng J-T, Teitelbaum P (1982) Reinstatement of festinating forward locomotion by antiserotonergic drugs in rats partially recovered from damage in the region of the nucleus reticularis tegmenti pontis. Exp Neurol 77:286–294.

Chesire RM, Cheng J-T, Teitelbaum P (1983) The inhibition of movement by morphine or haloperidol depends on an intact nucleus reticularis tegmenti pontis. Physiol. Behav. 30:809–818.

Chesselet M-F (1985) Somatostatinergic inputs to the region of the A8 cell group. Soc Neurosci Abstr 11:208.

Deutch AY, Goldstein M, Baldino F Jr, Roth RH (1988) Telencephalic projections of the A8 dopamine cell group. In: The mesocorticolimbic dopamine system (Kalivas PW, Nemeroff CB, eds), pp 27–50. New York: New York Academy of Sciences.

Garcia-Rill E, Skinner RD, Fitzgerald JA (1985) Chemical activation of the mesencephalic locomotor region. Brain Res 330:43–54.

George R, Haslett WL, Jenden DJ (1964) A cholinergic mechanism in the brainstem reticular formation: induction of paradoxical sleep. Int J Neuropharmacol 3:541–552.

Gerrits NM, Voogd J (1986) The nucleus reticularis tegmenti pontis and the adjacent rostral paramedian reticular formation: differential projections to the cerebellum and the caudal brain stem. Exp Brain Res 62:29–45.

Goldsmith M, van der Kooy D (1988) Separate non-cholinergic descending projections and cholinergic ascending projections from the nucleus tegmenti pedunculopontinus. Brain Res 445:386–391.

Hallanger AE, Wainer BH (1988) Ascending projections form the pedunculopontine tegmental nucleus and the adjacent mesopontine tegmentum in the rat. J Comp Neurol 274:483–515.

Hayakawa T, Zyo K (1986) Subcortical afferents to the nucleus reticularis tegmenti pontis in the rabbit: a retrograde horseradish peroxidase study. Okajimas Folia Anat Jpn 63:159–178.

Kanamori N, Sakai K, Jouvet M (1980) Neuronal activity specific to paradoxical sleep in the ventromedial medullary reticular formation of unrestrained cats. Brain Res 189:251–255.

Katayama Y, DeWitt DS, Becker EP, Hayes RL (1984) Behavioral evidence for cholinoceptive pontine inhibitory area: descending control of spinal motor output and sensory input. Brain Res 296:241–262.

Kelland MD, Asdourian D (1989) Pedunculopontine tegmental nucleus-induced inhibition of muscle activity in the rat. Behav Brain Res 34:213–234.

Lai YY, Siegel JM (1988) Medullary regions mediating atonia. J Neurosci 8:4790–4796.

Lai YY, Siegel JM, Wilson WJ (1987) Effect of blood pressure on changes in muscle tone produced by stimulation of the medial medulla. Am J Physiol 252:H1249–H1257.

Lee HJ, Rye DB, Hallanger AE, Levey AI, Wainer BH (1988) Cholinergic vs noncholinergic efferents from the mesopontine tegmentum to the extrapyramidal motor system nuclei. J Comp Neurol 275:469–492.

Magoun HW, Rhines R (1946) An inhibitory mechanism in the bulbar reticular formation. J Neurophysiol 9:165–171.

Mahowald MW, Schenck CH (1989) REM sleep behavior disorder. In: Principles and practice of sleep medicine (Kryger MH, Roth T, Dement WC, eds), pp 389–401. Philadelphia: Saunders.

Mefford IN, Baker TL, Boehme R, Foutz AS, Ciaranello RD, Barchas JD, Dement WC (1983) Narcolepsy: biogenic amine deficits in an animal model. Science 220:629–632.

Miller JD, Farber J, Gatz P, Roffwarg H, German DC (1983) Activity of mesencephalic dopamine and non-dopamine neurons across stages of sleep and waking in the rat. Brain Res 273:133–141.

Milner KL, Mogenson GJ (1988) Electrical and chemical activation of the mesencephalic and subthalamic locomotor regions in freely moving rats. Brain Res 452:273–285.

Mitani A, Ito K, Hallanger AE, Wainer BH, Kataoka K, McCarley RW (1988) Cholinergic projections from the laterodorsal and pedunculopontine tegmental nuclei to the pontine gigantocellular tegmental field in the cat. Brain Res 451:397–402.

Moon Edley S, Graybiel AM (1983) The afferent and efferent connections of the feline nucleus tegmenti pedunculopontinus, pars compacta. J Comp Neurol 217:187–215.

Morales FR, Engelhardt JK, Soja PJ, Pereda AE, Chase MH (1987) Motoneuron properties during motor inhibition produced by microinjection of carbachol into the pontine reticular formation of the decerebrate cat. J Neurophysiol 57:1118–1129.

Morrison AR (1983) A window on the sleeping brain. Sci Am 248: 94–102.

Preston RJ, McCrea RA, Chang HT, Kitai ST (1981) Anatomy and physiology of substantia nigra and retrorubral neurons studied by extra- and intracellular recording and by horseradish peroxidase labeling. Neuroscience 6:331–344.

Sakai K, Sastre J-P, Salvert D, Touret M, Tohyama M, Jouvet M (1979) Tegmentoreticular projections with special reference to the muscular atonia during paradoxical sleep in the cat: an HRP study. Brain Res 176:233–354.

Sakai K, Sastre J-P, Kanamori N, Jouvet M (1981) State-specific neurons in the ponto-medullary reticular formation with special reference to the postural atonia during paradoxical sleep in the cat. In: Brain mechanisms and perceptual awareness (Pompeiano O, Ajmone Marsan C, eds), pp 405–429. New York: Raven.

Schenkel E, Siegel JM (1989) REM sleep without atonia after lesions of the medial medulla. Neurosci Lett 98:159–165.

Shik ML, Severin FV, Orlovsky GN (1966) Control of walking and running by means of electrical stimulation of the midbrain. Biophysics 11:756–765.

Shiromani PJ, Siegel JM, Tomaszewski KS, McGinty DJ (1986) Alterations in blood pressure and REM sleep after pontine carbachol microinfusion. Exp Neurol 91:285–292.

Shiromani PJ, Armstrong DM, Gillin JC (1988) Cholinergic neurons from the dorsolateral pons project to the medial pons: a WGA-HRP and choline acetyltransferase immunohistochemical study. Neurosci Lett 95:19–23.

Shiromani PJ, Lai YY, Siegel JM (1990) Descending projections from the dorsolateral pontine tegmentum to the paramedian reticular nucleus of the caudal medulla in the cat. Brain Res (in press).

Siegel JM (1979) Behavioral functions of the reticular formation. Brain Res Rev 1:69–105.

Siegel JM, Tomaszewski KS, Fahringer H, Kilduff T, Dement WC (1989) Heart rate and blood pressure changes during sleep-waking cycles and cataplexy in narcoleptic dogs. Am J Physiol 256:H111–H119.

Sinnamon HM (1984) Forelimb and hindlimb stepping by the anesthetized rat elicited by electrical stimulation of the diencephalon and mesencephalon. Physiol Rev 33:191–199.

Steinfels GF, Heym J, Strecker RE, Jacobs BL (1983) Behavioral correlates of dopaminergic unit activity in freely moving cats. Brain Res 258:217–228.

Tohyama M, Sakai K, Salvert D, Touret M, Jouvet M (1979) Spinal projections from the lower brain stem in the cat as demonstrated by the horseradish peroxidase technique. I. Origins of the reticulospinal tracts and their funicular trajectories. Brain Res 173:383–403.

Vertes RP, Martin GF (1988) Autoradiographic analysis of ascending projections from the pontine and mesencephalic reticular formation and the median raphe nucleus in the rat. J Comp Neurol 275:511–541.

Wallace DM, Magnuson DJ, Gray TS (1989) The amygdalo-brainstem pathway: selective innervation of dopaminergic, noradrenergic and adrenergic cells in the rat. Neurosci Lett 97:252–258.

Webster HH, Jones BE (1988) Neurotoxic lesions of the dorsolateral pontomesencephalic tegmentum-cholinergic cell area in the cat. II. Effects upon sleep-waking states. Brain Res 458:285–302.